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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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JEFFRY S. MANN, PH.D.
MORGAN, LEWIS & BOCKIUS LLP
ONE MARKET, SPEAR STREET TOWER
SAN FRANCISCO, CA 94105

EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,047	MEARES ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-29* is/are pending in the application.

4a) Of the above claim(s) *16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-15 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Meares et al.

Response to the Amendment

The Amendment filed on 12/27/2005 in response to the previous Non-Final Office Action (06/22/2005) is acknowledged and has been entered.

Claims 1-8 and 10-29 are currently pending.

Claims 16-23 have been withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-8, 10-15 and 24-27 are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 10-15 remain and new claims 28-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of antibodies comprising an antigen recognition domain that recognizes a genus of macrocyclic metal chelate and a targeting moiety that binds specifically to a cancer cell. Thus, the claims are broadly drawn to antibodies defined solely by their antigen recognition domain for any macrocyclic metal chelate, which is simply a wish to know the identity of any material with that binding property. However, the written description in this case only sets forth an antibody referred to as 2D12.5

comprising an antigen recognition domain that recognizes one sub genus of macrocyclic metal chelate represented in claim 6 and a targeting moiety that binds specifically to a cancer cell.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 5, lines 10-14) that specific antibodies of the invention include, but are not limited to, antibodies that recognize and bind to an array of macrocyclic metal chelate which are structurally distinct, wherein the "promiscuity" of the antibodies is a unique feature. With regards to the macrocyclic metal chelate, the specification teaches (page 4, lines 30-31) that metal chelates include not only metal chelates comprising all carbons, but also any metal chelate comprising four heteroatoms such as O, S, N and/or any combination thereof. With regards to the a N substituted macrocyclic metal chelate, the specification teaches (page 56, paragraph 0236 to 0237) that the metal chelate may include a substituted or unsubstituted ethyl bridge that covalently links at least two of the nitrogen atoms as represented in the formula shown on page 56 of the specification. However, the written description (specification, page 66 to 69) only reasonably conveys one species of antibody (2D12.5) comprising a recognition domain that recognizes a macrocyclic metal chelates represented on page 57 (claim 6); and therefore, is not commensurate with any and/or all antibodies comprising an antigen recognition domain that recognizes any and/or all macrocyclic metal chelates. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a

substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of antibodies that encompass the genus of antibodies that comprise a recognition domain which recognizes a macrocyclic metal chelate nor does it provide a description of structural features that are common to the antagonists. Further, the specification fails to provide a representative number of macrocyclic metal chelates that encompass the genus for which are recognized by an antibody along with a description of structural features that are common to the macrocyclic metal chelates. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of antibodies and metal chelates for which they recognize, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or

simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only forth an antibody referred to as 2D12.5 comprising an antigen recognition domain that recognizes a macrocyclic metal chelate represented in claim 6, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to this rejection, Applicants contend that the written description requirement is satisfied when a representative number of species of the claimed invention are described. Applicants further assert that this principal is exemplified by In re Herschler 200 USPQ 711 (CCPA 1979) ("herschler"); MPEP 2163(II)(A)3)(a)(ii), wherein the Patent Office rejected the claims drawn to the use of DMSO to enhance delivery of physiologically active steroids for lacking written description because the specification did not disclose a representative number of physiologically active steroids. However, the CCPA reversed the Patent Office's rejection of these claims, reasoning that, because the invention was not the discovery of novel steroidal agents but a method of delivering the agents in combination with DMSO, explicitly written disclosure of all steroidal agents was not required to meet the written description requirement. Therefore, Applicants argue that the written description requirement does not require all species of every claim term to be disclosed; rather, only adequate description of the claimed invention. In the present case, Applicants submit that the claimed invention is not a mutant antibody, but a novel method of using these mutant antibodies to treat cancer. As shown in Herschler, Applicants contend that one example can adequately describe the claimed methods for written description purposes. For example, Applicants argue that they have described the use of antibodies, such as 2D12.5, in methods of treating cancer on pages 60-63 of the specification.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants contention that, just as in *Heschler*, the written description requirement does not require all species of every claim term to be disclosed, the Examiner acknowledges and agrees with Applicant's interpretation of *Herschler* in that the written description requirement does not require all species of every claim term to be disclosed. However, the Examiner recognizes that the fact patterns involved in *In re Herschler* appear to be different from those in the present application. In Herschler, the appellant has found that DMSO enhances the penetration of a number of materials through skin tissue. As such, the "novelty" of Herschler's invention appears to be the use of DMSO combination with steroidal agents as a method of enhancing the delivering these agents. In the instant case, the claims are drawn to a method of treating cancer comprising administering a genus of antibodies which has a recognition domain that recognizes a genus of macrocyclic chelate and attached to a genus of targeting moieties that bind to a cancer cell. Thus, the "novelty" of the invention appears to be the genus of antibodies which can be used in a method of treating cancer with a macrocyclic chelate. However, the claims encompass a genus of molecules defined solely by its principal biological property, which is simply a wish to know the identity of any material with that biological property. Accordingly, there is insufficient written description encompassing a "antibody comprising an antigen recognition domain that recognizes a macrocyclic chelate useful for treating cancer" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of a "antibody" are not set forth in the specification as-filed, commensurate in scope with the claimed invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116). In response to Applicants submission that the claimed invention is not a mutant antibody, but a novel method of using these mutant antibodies to treat cancer, it is noted that the features upon which applicant relies (i.e., mutant antibody) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 1-8, 10-15 and 24-27 remain and new claims 28-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification and prior art, while being enabling for a method of treating cancer in a subject comprising administering an antibody comprising an antigen recognition domain that recognizes a macrocyclic metal chelate such as DOTA, wherein said antibody comprises a targeting moiety, anti-CEA, that binds to a cancer cell by binding with a cell surface antigen; and administering to said subject a metal chelate, does not reasonably provide enablement for a method of treating any cancer in a subject comprising administering an any and/or all antibodies comprising an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises any and/or all targeting moieties which binds to a cancer cell by binding to any and/or all cell surface receptors and cell surface antigens; and a macrocyclic metal chelate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant claims read a method of treating cancer in a subject comprising administering to said subject an antibody that comprises an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises a targeting moiety which binds to a cancer cell by binding to a cell surface receptors and cell surface antigens. Thus, the claims read on a method of treating any cancer in a subject comprising administering to the subject any and/or all antibodies

comprising an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises any and/or all targeting moieties which binds to a cancer cell by binding to any and/or all cell surface receptors and cell surface antigens; and administering a macrocyclic metal chelate.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn a method of treating any cancer in a subject comprising administering to the subject any and/or all antibodies comprising an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises any and/or all targeting moieties which binds to a cancer cell by binding to any and/or all cell surface receptors and cell surface antigens; and administering a macrocyclic metal chelate. The specification teaches (page 61, lines 1-9) that patients suffering from a disease or condition, such as cancer, can be treated via the steps of: (a) administering to the patient an antibody comprising; (i) an antigen recognition domain that specifically binds to the metal chelate and (ii) a targeting moiety that binds specifically to a cell by binding with a surface group; and (iii) a metal chelate, wherein the metal chelate and antibody bind to form an antibody-antigen pair. The specification further provides (Example 3, pages66-68) a monoclonal antibody, 2D12.5, which shows broad specificity and high affinity for all rare earth metal DOTA complexes. However, the specification appears to be silent on any working examples, wherein a macrocyclic metal chelate and an antibody comprising: (1) an antigen recognition domain that recognizes a macrocyclic metal chelate; (2) a targeting moiety which binds to a cancer cell are administered to a subject for the treatment of cancer. Specifically, the specification does not appear to suggest any variables such as the dose of either the antibody or metal chelate, the dose rate delivered, the tumor size, routes of administration, the times between administration, the radiosensitivity, or what the targeting moiety is.

Thus, the instant specification provides insufficient guidance and objective evidence to predictably enable one of skill in the art to use the invention as claimed. Although the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). Those of skill in the art would recognize the

unpredictability of radioimmunotherapy. For example, Lovqvist *et al.* (J. Nucl. Med. 1998; 39: 1776-1777) discloses caveats and cautions in using pretargeting as a way of delivery radionucleotides selectively to tumors. These cautions include: (1) the immunogenicity of compounds such as streptavidin; (2) the presence of endogeneous biotin; (3) the rapid tumor clearance of monovalent chelates; (4) the restriction in using antibodies against chelates with limited nuclide applicability; and finally, (5) racemic mixtures of chelates may have a variable effect, wherein the enantiomeric nature influences targeting (page 1777, 1st column, 2nd paragraph). Lovquist *et al.* further teaches that while some progress has been made to address these points, the authors question whether this will be good enough quoting from Zhu et al (J. Nucl. Med. 1998; 39: 65-76) whom stated "pretargeting ... was neither sensitive enough for radioimmunodetection nor effective enough for radiotherapy" (page 1777, 1st column, 3rd-4th paragraph). Moreover, Goodwin *et al.* (Cancer 1997; 80: 2675-2680) discloses comparisons between the 3 step pretargeting method and the presently claimed 2 step pretargeting method (3 step outlined in Figure 1, page 2676). Goodwin *et al.* teach that pretargeting without the chase step, as in the presently claimed invention, requires a long waiting period for the blood MoAb concentration to fall, because even small amounts of MoAb remaining in the blood will immediately bind the effector molecules upon injection (page 2678, 1st column, 2nd paragraph to 2nd column). Thus, the teachings of Goodwin *et al.* stress the relationship between the time that the antibody is first administered and the second administration of the radionucleotide, i.e., the macrocyclic metal chelate. In addition to the time dependence discussed, *supra*, Goodwin *et al.* further disclose that many other question pertaining to pretargeting still remain unanswered such as optimal dosing schedule, molecular weight, valency, affinity constants, specific activity, rates of metabolism, and antigen modulation (Table 5, page 2679). More recently, Goldberg *et al.* (Cancer Immunol. Immunother. 2003; 52: 281-296) discloses the advancing role of radiolabeled antibodies in the therapy of cancer and the use of pretargeting strategies such as bispecific antibodies for the delivery of radionucleotides to enhance tumor to non-tumor ratios (abstract). In concurrence with Goodwin *et al.*, Goldberg *et al.* teach that the timing of the second injection of the radionucleotide is important, in order to achieve high tumor-to-background ratio when there is little to no bsAb circulating in the blood (page 285, 1st column, 1st paragraph). All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art such as radioimmunotherapy.

Therefore, in view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

In response to this rejection, Applicants contend that they have provided adequate teachings on how to make and use antibodies of the invention for treating cancer see specification pages 60-63. As such, Applicants contend that they have complied with the enablement requirement as described by the MPEP.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants contention that they have provided adequate teachings in the specification (pages 60-63) on how to make and use antibodies of the invention for treating cancer, the Examiner acknowledges what the specification. However, the Examiner recognizes that those of skill in the art recognize the unpredictability of radioimmunotherapy as evidenced by the references cited above. In view of these teachings, and the lack of guidance and or exemplification in the specification, it would not be predictable that the method would function as contemplated. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Applicant's arguments, see page 12, filed 12/26/2005, with respect to the rejection(s) of claim(s) 1-8, 10-14 and 24-27 under 35 USC 102 (a) as being anticipated by Sharkey et al. (2002 ASCO Annual Meeting abstract, Orlando, Fl., May 18, 2002) and under 35 USC 102(b) as being anticipated by Hansen et al. (US 2002/0006379, 2002) have been fully considered and are persuasive because neither of the reference teach or suggest Applicant's element of "antigen recognition domain that recognizes a macrocyclic chelate" (Remarks, page 12). Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made.

New Rejections upon further consideration:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10-15 and 24-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (WO 99/66951).

Hansen et al. teach a method of treating diseased tissues in a patient, comprising: (a) administering to a patient a bi-specific antibody or antibody fragment having at least one arm that specifically binds to a targeted tissue and at least one arm that specifically binds a targetable conjugate; (b) optionally, administering to said patient a clearing composition, and allowing said composition to clear non-localized antibodies or antibody fragments from circulation; and (c) administering to said patient a first targetable conjugate which comprises a carrier portion which comprises or bears at least one epitope recognizable by said at least one other arm of said bi-specific antibody or antibody fragment, and one or more therapeutic agents (page 58, claim 1 of WO document). With regards to the targetable conjugate's epitope, the WO document teaches (page 9, lines 30-33) that the epitope includes, but is not limited to, a hapten. With regards to the hapten, Hansen et al. teach (page 10, line 2 and page 34, lines 27-28) that haptens include, but are not limited to, chelators such as DPTA and DOTA. For example, the WO document teaches (page 35, lines 7-11) a method of treating CEA-expresing tumors, wherein a bi-specific antibody with at least one arm, which specifically binds to CEA, and at least one arm, which specifically binds the targetable conjugate whose hapten is a conjugate of yittruim-DOTA is administered to a patient. With regards to the bi-specific antibody which recognizes CEA and a metal chelate such as DOTA, the WO document teaches (page 10, lines 26-33) that the bi-specific antibody is generated by derivatizing an anti-CEA $F(ab')_2$ mAB with a hydrazide-maleimide cross-linker and coupling said derivatized anti-CEA $F(ab')_2$ to an anti-chelate Fab'-SH. Moreover, Hansen et al. teach (page 24, lines 24-33) that chelators, such as DOTA, may be conjugated to the carrier portion of a targetable conjugate by generating a reactive functional group such as carbodiimide and coupling the carbodiimide to the peptides free amines. Thus, while Hansen et al. does not teach a macrocyclic metal chelate comprising four nitrogen atoms, wherein at least two of the nitrogen atoms are covalently linked to a substituted or unsubstituted ethyl bridge or comprise a subunit shown in claim 4 or a formula of claim 6 or an S configuration DOTA, the referenced limitations are an inherent structural feature of DOTA as evidenced by Sigma-Aldrich (see attached document of record). Thus, the claimed

antibody appears to recognize the same macrocyclic metal chelate as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that a product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Therefore, No claim is allowed.

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
3/20/06